that systolic dysfunction is common in DHF. Methods: Echocardiography with tissue Doppler imaging was performed in 339 subjects, in whom 92 had systolic heart failure (SHF) (ejection fraction <50%), 73 had DHF (ejection fraction =>50% with diastolic abnormalities on Doppler echocardiography), 68 had isolated diastolic dysfunction (DD) and 106 normal controls. Regional myocardial velocity curves were constructed offline using a 6-basal, 6-mid segmental model. Results: The peak regional myocardial sustained systolic (Sm) and early diastolic (Em) velocities were significantly lower in patients with SHF, DHF and DD than controls in almost all the myocardial segments. Likewise, the mean Sm (SHF < DHF < DD < Controls: 3.3 ± 1.0 < 4.6 ± 1.3 < 5.4 ± 1.0 < 6.3 ± 1.0 cm/s; all p <= 0.001) and mean Em (SHF = DHF < DD < Controls; 3.6 ± 1.2 = 3.9 ± 1.3 < 5.3 ± 1.6 < 7.2 ± 1.7 cm/s; all p < 0.001) from the six basal segments were decreased in all the disease groups. A mean Sm of 4.4 cm/s (-2 standard deviation of controls) predicted the presence of systolic dysfunction in 92% of patients with SHF, 52% with DHF and 14% with DD. Conclusions: Using tissue Doppler imaging, systolic abnormalities were evident in patients previously labeled as DHF, and to a much lesser extent, isolated DD. This indicates the common coexistence of systolic and diastolic dysfunction in a spectrum of different severity in the pathophysiologic process of heart failure.

1157-155 Prevalence, Clinical Characteristics, Quality of Life, and Prognosis of Patients With Congestive Heart Failure and Isolated Diastolic Dysfunction

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Background. Prevalence of isolated LV diastolic dysfunction (IDD) has been reported to be as high as 1/3 of all chronic congestive heart failure (CHF) cases, with an increasing prevalence in the elderly population. However, there is a paucity of prospective data about the prevalence and prognosis of IDD in an unselected population of pts admitted to hospital with CHF.

Methods. We prospectively evaluated 179 consecutive pts admitted in medical departments of our hospital for CHF. Among them, 135 (59% males, median age 74 years) showed sinus rhythm, and no significant valvulopathy (except heart valve prosthesis or secondary mitral regurgitation). CHF was diagnosed using a modification of the Framingham criteria, and IDD according to the European Study Group on Diastolic Heart Failure echo criteria (Eur Heart J 1998;19: 990). Six-month survival of CHF pts was compared with that of age- and sex-matched general population living in Udine in 1995.

Results. Twenty-nine pts (22%) had IDD; 102 (76%) LV systolic dysfunction (i.e. LV ejection fraction <45%. There was no difference in age, gender and NYHA functional class between pts with IDD or LV systolic dysfunction. Six-month rehospitalisation rate (50% and 48%) and median in-hospital length-of-stay during readmissions (10 and 10 days) was similar between the 2 groups. Using the Minnesota Living with Heart Failure score, quality of life was similar between the 2 CHF pt groups both at discharge (39.4 and 34), and at 6-month visit (10.4 and 10.4). Six-month survival, adjusted for age and gender, was similar between pts with IDD or LV systolic dysfunction (90% and 89.8%, Hazard Ratio= 0.99; 95%CI 0.27-3.61), and significantly reduced (Log Rank= 8.58; p<0.001) in comparison to that of the general population (Figure). Two pts (7% of pts with LV ejection fraction< 45%) did not show any echo evidence of cardiac dysfunction.

Conclusions: our data show that, using standardized echo diagnostic criteria, prevalence of IDD in pts admitted to hospital with CHF seems to be lower than previously reported. CHF pts with IDD showed clinical symptoms, self-perceived quality of life, re-hospitalization rate, and 6-month mortality similar to pts with prevalent systolic dysfunction.

1157-156 What Is Late Mortality After Hospitalization for Heart Failure in the Real World? A One-Year Report From the Lady Davis Carmel Medical Center Registry

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Background: Heart failure (CHF) is common cause of morbidity and mortality but current prevalence and long-term outcome are largely unknown in general population as opposed to pts selected for clinical trials.

Patients and Methods: 362 consecutive pts discharged from hospital with clinical CHF or suspected CHF (drug treatment compatible with CHF/LV dysfunction) were enrolled in CHF registry by prospective screening of internal medical, cardiac, intensive care and cardiac surgical departments in 2 hospitals (1 tertiary center with cardiac surgery, 1 referral hospital) over 6 week period in each. Survival status at 1 yr was ascertained by telephone and from governmental records.

Results: A quarter (90/362, 25%) of CHF pts died within 12 mths, a death rate higher than that reported in most recent clinical CHF trials. Pts who died were older (77±10 vs 75±11 yrs, p=0.03), but death was not predicted by new acute myocardial infarction (AMI) or new atrial fibrillation (AF)/paroxysmal AF at time of entry to registry or by presence of diabetes mellitus (31/90, 34% vs 74/272, 27%, NS), nor following correction for age and sex in stepwise multivariate model.

Conclusions: In pts hospitalized for CHF or suspected CHF in the real world: 1. Late (12 mth) mortality was higher than expected. 2. Mortality was higher in older pts. 3. Death was not predicted by acute event at entry to database and was marginally but not significantly higher in diabetics.

Predictors of 1 year mortality

Vital status (12 mths)	Age (yrs)	AMI on index admission	New AF/PAF on index admission	IDDM	NIDDM
Dead (N=90)	77±10	6 (7%)	7 (8%)	7 (8%)	24 (27%)
Alive (N=272)	75±11	21 (8%)	24 (9%)	21 (8%)	53 (20%)
p value	0.03	NS	NS	NS	NS

1157-157 Impaired Left Ventricular Filling Predicts Augmented Ventilatory Response to Exercise in Patients With Chronic Heart Failure

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Introduction. Augmented ventilatory response to exercise (VE/VCO_2 slope) well predicts poor prognosis in chronic heart failure (CHF). However, the mechanisms responsible for exercise hyperpnea in CHF have not been fully elucidated. The aim of this study was to determine the interrelationship between resting ECHO 2D-derived parameters and elevated VE/VCO_2 slope in CHF. **Methods and results**. In 38 stable CHF patients (33 men, 63±8 years, NYHA class II/III 26/12) prospective ECHO-2D examination (mean end diastolic diameter [EDD]: 68±8 mm, shortening fraction [SF]: 16±7%) followed by cardiopulmonary exercise testing (peak oxygen consumption: [peakVO_2]: 19.0±6.3 ml/min/kg, VE/VCO_2 slope 37.6±12.7). VE/VCO_2 slope correlated with the following echocardiographic parameters: short isovolumic relaxation time (IVRT, r=-0.47, p=0.005), decreased mitral A wave peak velocity (A_{vel}, r=-0.44, p=0.006), depressed right ventricle long axis function (RV excursion, r=-0.37, p=0.03), and left ventricular restrictive filling pattern (defined as mitral E/A ratio > 1 and deceleration time ≤120ms, r=0.47, p=0.004). There was no relationship between resting ECHO-2D indices and peak VO_2. Twenty (53%) pts with high VE/VCO_2 i.e. > 34.0) were identified: (table).

	EDD (mm)	SF(%)	A_{vel} (m/s)	IVRT (ms)	RV excursion (mm)	Restrictive mitral flow (%)
High VE/VCO_2 (n=20)	68±8	17±7	0.4±0.3**	24±59 *	12±4*	65*
Normal VE/VCO_2 (n=18)	68±8	18±7	0.8±0.3	60±25	17±4	29

Mean ± SD, *p<0.05, **p<0.01 high vs normal VE/VCO_2**Conclusion:** In CHF impaired left ventricular filling pattern and depressed right ventricle long axis function may be important factors responsible for augmented ventilatory response to exercise.

1157-158 Efficacy and Tolerability of Carvedilol in Diabetic Patients With Chronic Heart Failure

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Background: The benefits of beta blockers (BB) in patients with chronic heart failure (CHF) are well established, however, there is limited data on the impact of BB in diabetic CHF patients, a subgroup in whom BB have been considered relatively contra-indicated. The aim of this study was to compare the efficacy and tolerability of the BB, carvedilol in diabetic and non-diabetic CHF patients.

Methods: A retrospective analysis was conducted on 505 consecutive patients with CHF (434 men, 71 women) aged 55±13 years who were commenced on carvedilol between February 1996 and May 2001. Ninety-three patients (18%) had a history of diabetes mellitus (DM group). Patients were reviewed at 3, 6, 12, 18 and 24 months then annually. Vital signs, NYHA functional class, 6 minute walk distance (6MWD), carvedilol dose and echocardiographic measurements of LV dimensions (LVEDD and LVESD) and fractional shortening (FS) were recorded at each visit. In addition, survival and non-fatal adverse events were recorded.

Results: There were no significant differences between the DM and non-DM groups at baseline with respect to age, sex, duration of CHF, heart rate, diastolic blood pressure, serum Na^+ and creatinine, drug therapy, NYHA class, LV dimensions and function. The DM group were significantly heavier, had lower 6MWD, and higher systolic blood pressure at baseline. A higher percentage of diabetics had ischemic heart disease (54% v 37%, p=0.007). During a mean follow up of 32±18 months, 22% of the DM group died, 12% underwent heart transplantation (HTx) and 11% withdrew from carvedilol due to adverse events. In comparison, 19% of the non-DM group died, 9% underwent HTx and 18% were withdrawn from carvedilol due to adverse events (all p=ns compared with DM group). Mean maintenance carvedilol doses were 42±2 and 39±3 mg/day for DM and non-DM groups (p=ns). At 24 months, NYHA class and 6MWD improved significantly, LVEDD fell by 3.1±0.5 mm, LVESD by 4.9±0.6 mm and FS rose by 3±1% (all p < 0.0001 versus baseline, n=226), with no significant differences between the DM and non-DM groups.

Conclusion: The tolerability, clinical outcomes and beneficial effects of carvedilol on LV remodelling are similar in diabetic and non-diabetic CHF patients.

1157-159 Is Additional Neurohormonal Antagonism Useful in Patients With Severe Chronic Heart Failure Already Receiving a Combination of Neurohormonal Antagonists? Results of the COPERNICUS Study

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Background. The results of the Val-HeFT study suggested that broad based neurohormonal blockade may have deleterious effects in patients with heart failure (HF), but this hypothesis has not been evaluated in other trials.

Methods. The 2289 patients with severe HF in the COPERNICUS trial were randomized to placebo (PBO) or carvedilol (CRV), which were added to diuretics and an ACE inhibitor (± digitalis) for up to 29 months. Of these patients, 445 were also on spironolactone at baseline and thus received 3 neurohormonal antagonists if they were randomized to CRV. Compared with those not on spironolactone, patients on spironolactone had a

lower blood pressure and serum Na and were more likely to have had a recent HF hospitalization (all P < 0.001). Results. Shown below are 1-year Kaplan-Meier rates and Cox model hazard ratios (CRV:PBO):

	Spironolactone			No Spironolactone		
	PBO (n=225)	CRV (n=220)	Hazard ratio	PBO(n=908)	CRV (n=936)	Hazard ratio
All-cause mortality	19.1%	11.4%	0.65	18.4%	11.3%	0.65
Death or hospitalization for worsening HF	39.3%	26.3%	0.63	37.5%	25.4%	0.70
Death or cardiovascular hospitalization	41.6%	29.1%	0.61	41.6%	30.4%	0.75
Death or any hospitalization	47.2%	38.4%	0.76	53.3%	42.1%	0.76

CRV reduced the risk of a major clinical event in patients on spironolactone to an extent similar to that seen in patients not on spironolactone.
Conclusion. These data indicate that the morbidity and mortality of patients with severe HF receiving drugs that interfere with more than one neurohormonal target can be reduced substantially with further neurohormonal antagonism (with CRV).

1157-160 Beta-Blocker Utilization in Heart Failure Patients: Experience From a Heart Failure Clinic

Ritesh Gupta, W.H. Wilson Tang, James B. Young, *Cleveland Clinic Foundation, Cleveland, Ohio.*

Background: Beta blockers (BB) reduce mortality in heart failure (HF) patients. Though, well tolerated in clinical trials, utilization rates in clinical settings have not been studied.
Methods: Retrospective analysis of 500 consecutive HF patients presenting to a HF clinic between 3/01 to 5/01 (mean age 61, 69% males, 53% ischemic, mean LVEF 27%). Chi-square test was utilized for subgroup analysis.
Results: 75% of patients had been given a BB trial and 69% were currently on BB. The use of BB was more in moderate (LVEF 20 - 40, n=236) compared to mild (LVEF >40, n = 92) and severe (LVEF <20, n =141) HF (73% vs. 60% and 65%, p=0.04). BB use also decreased with worsening NYHA class of HF symptoms (I 78%, II 72%, III & IV 60%, p=0.01). No difference in BB use by gender was seen (68% in males vs. 71%, p=0.5). Discontinuation rate was 6.8% and was not influenced by NYHA class (p=0.3). Down titration was required in 5.2%. Side effects leading to stopping or down titration, included dizziness (3.2%), fatigue (2.8%), hypotension (2.6%), bradycardia (2.0%), and others (1.4%). A contraindication could be identified in 44% of patients never tried on BB with respiratory disease being the most common in 33%, uncompensated state in 7%, A-V block in 1% and hypotension in 1.6%. Subgroup of diabetics had lower BB use than non diabetics(60% vs 73%, p=0.02) with more contraindications (36% vs. 18%, p < 0.01) and worse NYHA class (p= 0.03) though LVEF was similar (p=0.5). Trend towards lower BB use was seen in elderly patients (age >74) than younger patients (61% vs. 71%, p=0.06) but there was no difference in rate of contraindication to BB(29% vs. 23%, p= 0.1).
Conclusion: High utilization rates for BB (69% current usage) can be achieved with an aggressive approach to initiating BB therapy. Respiratory diseases are the most common reason of not initiating BB therapy. Diabetics and elderly patients are less likely to be on BB. Diabetics tend to have more contraindications to BB and worse NYHA class than non diabetics, which may explain lower use of BB in them. Elderly patients do not show this trend and lower use in this group needs further investigation.

POSTER SESSION

1158

Chagas, Diabetes, Scleroderma, and Cardiomyopathy

Tuesday, March 19, 2002, 9:00 a.m.-11:00 a.m.
Georgia World Congress Center, Hall G
Presentation Hour: 9:00 a.m.-10:00 a.m.

1158-146 Phosphoramidan Ameliorates the Functional Sequelae of Experimental Chronic Chagasic Cardiomyopathy

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Background. *Trypanosoma cruzi*, the etiologic agent of Chagas' disease, is an important cause of chronic cardiomyopathy. Coronary microvascular spasm, in part mediated by endothelin-1, appears to play a significant role in the pathogensis of experimental chronic chagasic cardiomyopathy. **Aim.** We sought to assess if the administration of an endothelin inhibitor, phosphoramidan, could influence the severity of cardiomyopathy in mice infected with *T. cruzi*. **Methods.** Therefore we infected cd1 mice (n=21) with 10^4 trypomastigotes of the Brazil strain of *T. cruzi*. Of these, 8 were treated with phosphoramidan. An additional 8 uninfected littermates served as controls (C), 3 of which received phosphoramidan. All mice (n=29) survived and were evaluated at 150 days post infection by transthoracic echocardiography. Left ventricular (LV) end diastolic diameter (EDD), relative wall thickness (RWT), and fractional shortening (FS) were measured. Right ventricular (RV) size was assessed semi-quantitatively on a scale of 0-3. **Results.** There was no effect of phosphoramidan on LV EDD, RWT, FS or RV in uninfected (C) mice. Infected, untreated mice (INF) had increased LV EDD (3.2±0.1 v 2.8±0.1mm, p<0.05), along with reduced FS (39±2 v 57±1%, p<0.05) and RWT (0.4±0.0 v 0.5±0.0, p<0.05), compared with C. Treatment with phosphoramidan reduced the magnitude of these changes, such that the infected, phosphoramidan treated mice (INF+P) had no significant differences in LV EDD (2.9±0.1 v 2.8±0.1mm), RWT (0.5±0.1 v 0.5±0.1), and FS (57±2 v 50±4%) compared with C mice. Similarly, RV was larger in INF compared with both C and INF+P mice (2.1±0.3 v 1.5±0.4, INF v INF+P respectively, p<0.01). **Conclusion.** These data indicate that phosphoramidan ameliorates the functional sequlae of experimental chronic chagasic cardiomyopathy.

1158-147 Molecular Epidemiology of Cardiac Actin Gene Mutations in Dilated Cardiomyopathy

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Background: Dilated cardiomyopathies (DCM) are characterized by a large ventricular dilatation and impaired systolic function. There is a strong genetic component in DCM, estimated to be present in approximately 20-30percent of cases. Mutations in exons 5 (Arg312His) and 6 (Glu361Gly) of cardiac actin gene (ACTC) have been reported in two families with DCM. Methods: In order to evaluate prevalence and characteristics of ACTC gene mutations in DCM, 62 patients from different ethnic backgrounds were studied: 17 with sporadic DCM, 45 with familial DCM (belonging to 31 unrelated families). Two patients with ischemic heart disease were used as controls. Genomic DNA was extracted from blood or explanted heart tissue using standard procedures. PCR products were generated from all 6 exons of the ACTC gene, allowing the inclusion of the exon/intron boundaries. Mutation analysis of all 6 exons was performed using denaturing high performance liquid chromatography (DHPLC) and sequence analysis. Results: No mutation was found in any of the six ACTC exons. A single nucleotide polymorphism was detected by DHPLC, and confirmed by sequence analysis in intron 5 (C-62T). Conclusions: ACTC mutations do not seem to be associated with DCM in our large population of familial and sporadic DCM. ACTC mutations appear to be infrequently associated with DCM.

1158-148 Noninvasive Assessment of Coronary Flow Reserve Impairment in Patients With Systemic Sclerosis

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Background. Systemic sclerosis (SSc) is a chronic connective tissue disorder of unknown etiology, characterized by cutaneous and visceral tissue fibrosis with arteriolar and capillary ischemic dysfunction . The pathogenesis of the cardiac lesion in SSc is controversial, but the primary disorder of microvasculature with diffuse arteriolar and capillary lesions could precede any fibrosis, thus causing ischemic disorder to the heart. CFR is used to evaluate coronary microcirculation, and has been already employed to investigate myocardial microcirculation impairment in SSc. Previous invasive studies have demonstrated that coronary flow reserve (CFR) is impaired in patients (pts) with advanced SS and cardiac involvement. We tested the hypothesis that CFR can be early impaired in patients with systemic sclerosis without cardiac involvement and whether CFR impairment is correlated to the cutaneous subset.
Methods. We studied 26 patients with SSc without clinical evidence of heart disease, (14 with diffuse form and 12 with localized form of SSc) and 22 control group patients, matched in age and gender. We evaluated CFR in the left anterior descending coronary artery (LAD) with a new non-invasive method : contrast (Levovist) enhanced transthoracic Doppler (CEE-TTE) during adenosine infusion. The pulsed wave Doppler of blood flow velocity was recorded in the LAD at rest and after maximum vasodilation by adenosine infusion (140 mcg/Kg/min in 5 minutes).
Results: In patients with SSc, without clinical evidence of heart disease, CFR was impaired (2.65±0.63 vs 3.29±0.52 in controls, p < 0.0005). A significantly , greater percentage of SSc patients had reduction of (≤ 2.5) CFR compared to controls (48% vs 4.5%, p=0.003). Left ventricular mass and ejection fraction were not statistically different in the two groups. A non-significant trend between mean CFR and the severity and duration of the disease was also observed.
Conclusion. In this cross-sectional study we demonstrated that CFR is early reduced in patients with SSc and seems to be correlated to the extension of the cutaneous subset of the disease. A reduction of CFR could be an early sign of cardiac involvement in systemic sclerosis.

1158-149 Clinical Course of Dilated Cardiomyopathy in Asymptomatic Patients Long-Term Treated With Beta-Blocking Agents: The Heart Muscle Disease Registry of Trieste

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No conclusive data are available on long-term effects of adding a beta-blocker (BB) to ACE-inhibitor (ACE-I) therapy in asymptomatic patients with dilated cardiomyopathy (DC).
Among 447 DC patients consecutively enlisted in the Heart Muscle Disease Registry of Trieste between 1986 and 2000, 307 (68.7%) had HF symptoms (NYHA II-IV, Group 1) while 140 (31.3%) were asymptomatic (NYHA I, Group 2) at enrolment. In Group 2, a previous history of HF was present in 71 patients (50.7%)(Group 2a) and absent in 69 (49.3%)(Group 2b).